PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 8702.110-304	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/14609	International filing date *(day/month/year)* 12 May 2003 (12.05.2003)	Priority date *(day/month/year)* 17 May 2002 (17.05.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 38/18, A61F 2/02 and US Cl.: 424/409, 418, 423; 514/12, 8, 21		
Applicant WYETH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 08 December 2003 (08.12.2003)	Date of completion of this report 13 April 2005 (13.04.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Jennifer Ione Harle J. Roberts for Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/14609

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-28 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the claims:
pages 29-38 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the drawings:
pages 1 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/14609

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 1-71	YES
	Claims NONE	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-71	NO
Industrial Applicability (IA)	Claims 1-71	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/14609

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. Citations and Explanations:
Claims 1-13 lack an inventive step under PCT Article 33(3) as being obvious over Valentini et al. (US 5,929,984).

The instant claims are drawn to a composition having functional intended use. The scaffolding is formed from the mixed solution by drying from the wet state, preferably by lyophilization without freezing (column 7, lines 22-24). Hence, it is clear that prior to drying, Valentini et al. (US 5,939,974) disclose a solution that meets the limitations of the instant claims. The same preferred hyaluronic acid esters - HYAFF®, the s ame pore-forming agents, the same tricalcium phosphate and several of the same BMPs, and the same solubilizing organic solvents are explicitly recited as being parts of this composition. There is no indication that the solutions are not injectable, just that it is preferred to dry the solutions to form an implantable porous scaffold.

Claims 1-71 lack an inventive step under PCT Article 33(3) as being obvious over
Valentini et al. (US 5,939,974) in view of Wozney et al. (US 6,187,742) and Walter et al. (US 5,716,413) and further in view of Pheulpin (US 3,955,719), Langen et al. (US 4,784,055) and Phillips et al. (US 4,758,233).

The teachings of Valentini et al. (US 5,939,974) have been discussed above. Valentini et al. (US 5,939,974) lack BMP-7 (instantly called OP-1.

Wozney et al.(US 6187742) teach the combination of osteogenic proteins (including BMP-7, which is OP-1, and preferably BMP-2; (column 3, lines 26-50) with a number of carriers including porous particulate polymers (including PEG; column 4, line 59- column 5 line 5), sucrose (column 5, lines 40-42), hyaluronic acid and tricalcium phosphate (column 5, lines 50-56). Wozney et al. discuss the use of the preparation by injection through a syringe (column 5 line 63).

Pheulpin (US 3,955,719) discloses a device and methods for injecting pastes of dental products into cavities (abstract), albeit not through the skin.

Walter et al. (US 5,716,413) disclose that it is known in the art of bone repair to prepare a biodegradable, porous prosthesis in cylindrical as well as many other moldable forms.

Langen et al. (US 4,784,055) discloses a device and methods for injecting compositions having paste-like consistency through needles into meat. If the surface of the meat is considered its "skin", this method and device would clearly suffice to make such an injection.

Phillips et al. (US 4,758,233) disclose a device and methods to inject a medicament in the form of a cream or paste into an animal (column 1, lines 4-8). This clearly implies injecting at least through the skin.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

A person of ordinary skill in the art at the time the invention was made would have been motivated to substitute the BMP-7 as taught by Wozney et al. (US 6,187,742) for the BMPs in the composition as taught by Valentini et al. (US 5,939,974) because Wozney et al. (6,187,742) disclose that their BMPs can be formulated into carriers including porous particulate polymers, hyaluronic acid and TCP.

BMPs have been formulated with a range of suitable carriers. The only requirement for formulation appears to be compatibility with the bone matrix to which it is being added. Hence, given that the carriers of Wozney et al. (US 6,187,742) are functionally equivalent and nearly the same as those of Valentini et al. (US 5,939,974) (hyaluronic acid as compared to hyaluronic acid esters) it would involve nothing more than an arbitrary matter of experimental design choice to select one carrier over another. Such a choice is within the skill of the ordinary artisan of bone repairs. Pheulpin (US 3,955,719), Langen et al. (US 4,784,055) and Phillips et al. (US 4,758,233) are provided to further establish that pastes are injectable even through the skin.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the BMP-7 of Wozney et al. (US 6,187,742) for the BMPs in the composition as taught by Valentini et al. (US 5,939,974) and to inject the paste, even through the skin.

Claims 1-71 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

----------NEW CITATIONS----------
US 5,716,413 A (WALTER et al.) 10 February 1998 (10.02.1998), see entire document.